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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/724,538	11/28/2000	Daniel D. Shoemaker	9301-123	7044

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EXAMINER
LU, FRANK WEI MIN

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 10/03/2002

11

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/724,538	SHOEMAKER ET AL.	
	Examiner	Art Unit	
	Frank W Lu	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 June 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-36,45,46,86-90,157-183 and 212-279* is/are pending in the application.

4a) Of the above claim(s) *46,88,212,213,224,236,248,260,262,266,267,269,270,272,273,275,276,278 and 279* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-33,35,36,45,86,87,89,90,157-180,182,183,214,216,218-223,225,238,240,242-247,249,261,* ~~*and*~~ *263* is/are rejected. 1, 265, 268, and 274

7)☒ Claim(s) *3,34,181,215,217,226-235,237,239,241,250-259,264,271 and 277* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 November 2000* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7.5 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restriction

1. Applicant's election of species human and species " perturbation is exposure to a drug in Paper No. 9 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 35, 36, 182, 183, and 263 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

4. Claims 35, 36, 182, and 183 are rejected as vague and indefinite in view of the phrase "wherein said expression levels are measured as continuous variables" in claims 35, 36, 182, and 183 because it is unclear what it intended. For example, does this phrase mean said expression levels remain continuously change or this phrase mean something else? Please clarify.

5. Claim 263 is rejected as vague and indefinite in view of the phrase "the longest variant of an exon" because it is unclear what it intended. Does this phrase mean that the variant has the longest exon or this phrase mean something else? Pleas clarify.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

7. Claims 1, 4-6, and 45 are rejected under 35 U.S.C. 102(e) as being anticipated by DeRisi *et al.,* (Nature Genetics, 14, 457-460, 1996).

DeRisi *et al.,* teach use of cDNA microassay to analyze expression patterns in human cancer. They prepared fluorescence cDNA using mRNA from human tumorigenic UACC-903 and non-tumorigenic UACC-903(+6) by labeling with a green and red fluor respectively. These cDNAs was hybridized with an array including 870 different cDNAs and control. Several genes including p53 showed significant differences in expression between two cells (see pages 457 and 458). Note that: (1) cDNA from two different cells were considered to have a plurality of different genes having multiexons as recited in claim 1; (2) like claim 1, DeRisi *et al.,*did not

average the measured expression level of each exon or multiexons; and (3) it was known that p53 had at least 5 different exons as recited in claims 4-6.

Therefore, DeRisi *et al.,* teach all limitations recited in claims 1, 4-6, and 45.

8. Claims 7-9 are rejected under 35 U.S.C. 102(b) as being anticipated by DeRisi *et al.,* (1996) as applied to claims 1, 4-6, and 45 above, in light of Roninson *et al.,* (US Patent No.5,811,234, published on September 22, 1998).

The teachings of DeRisi *et al.,* have been summarized previously, *supra.* However, DeRisi *et al.,* did not disclose to a cDNA library having at least 100-10,000 different genes as recited in claims 7-9. Since Roninson *et al.,* showed that somatic tissues of higher eukaryotes expressed mRNA for about 10,000 genes (see example 9 in columns 15 and 16), a cDNA library made by DeRisi *et al.,* also considered to have 10,000 different genes as recited in claims 7-9.

9. Claims 1, 2, 10-12, 22-26, 28-33, 45, 86, 87, 89, 90, 157-159, 169-173, 175-180, 214, 216, 219-221, 223, 225, 238, 240, 243-245, 247, 249, 265, 268, and 274 are rejected under 35 U.S.C. 102(e) as being anticipated by Friend *et al.,* (US Patent No. 6,165,709, filed on February 26, 1998).

Regarding claims 1, 86, 89,, and 90, Friend *et al.,*teach transcript arrays for analyzing the transcriptional state in a cell, and especially for comparing the transcriptional states of two cells wherein a first cell that was exposed to a drug and a second cell that was not drug-treated. cDNA from two different cells were labeled with different fluorescence dyes and hybridized with a microarray with immobilized nucleic acid probes. When the drug treatment had no effect, either directly or indirectly, on the relative abundance of a particular mRNA in a cell, the mRNA levels

were equally prevalent in both cells. When the drug treatment had an effect, either directly or indirectly, on the relative abundance of a particular mRNA in a cell, the ratio of the first fluorescence dye to the second fluorescence dyes either increased or decreased (see columns 27-29 and 49-52). Note that: (1) cDNA from two different cells were considered to have a plurality of different genes having multiexons as recited in claim 1; (2) like claim 1, Friend *et al.*, did not average the measured expression level of each exon or multiexons; (3) drug exposure to the cell was considered as a perturbation.

Regarding claim 2, Friend *et al.*, teach to compare the transcriptional states of two cells wherein first cell in which a single gene was disrupted and a second cell in which the gene was not disrupted. Figure 3 B showed the hybridization patterns of the first cell in which a single gene was disrupted (see columns 27-29 and 49-52). Deletion mutant was confirmed due to lack of expression of disrupted gene in the cell. Deletion mutant was considered to have a distinguishing structural characteristic and cDNA from two different cells were considered to have a plurality of different genes having multiexons.

Regarding claims 10, 157, 214, and 238, the binding sites of the microarray were DNA polynucleotides corresponding to at least a portion of each gene in an organism's genome. These DNAs were obtained by polymerase chain reaction (PCR) amplification of gene segments from genomic DNA, cDNA (e.g., by RT-PCR), or cloned sequences. For example, based on the known sequence of the genes or cDNA, chosen PCR primers were generated unique fragments (i.e. fragments that do not share more than 10 bases of contiguous identical sequence with any other fragment on the microarray) (see columns 29 and 30). An array immobilized these unique

PCR fragments was considered as an array comprising a plurality of polynucleotide probes of different nucleotide sequences bound to different regions of a support wherein each of said different nucleotide sequences comprising a sequence complementary and hybridizable to a sequence in a multiexon. Here a multiexon was considered as a PCR product having two or more exons.

Regarding claims 11, 12, 158, and 159, it was known that some genes from yeast had at least 5 different exons.

Regarding claims 22-26, 169-173, 219-221, and 243-245, each gene fragment on the microarray was between about 50 bp and about 2000 bp, more typically between about 100 bp and about 1000 bp, and usually between about 300 bp and about 800 bp in length (see column 30, first paragraph).

Regarding claims 28-33, 175-180, 216, and 240, since claims 28-33 and 175-180 did not require that a sequence in the probe was fully complementary to a full length exon as recited in claims 30 and 177 or a multiexon as recited in claims 31 and 178 or a sequence spanning the splice junction between different exons as recited in claims 32,179, and 240 or sequence from adjacent exon as recited in claims 33 and 180, at least one nucleotide in these unique PCR fragments could hybridize to the sequence as recited in claims 30-33, 177-180, 216, and 240 and any size of sequence between any two complementary bases of the probe was considered as a linker as recited in claims 28 and 175 and any two complementary bases of the probe could located in different exons as recited in claims 29 and 176 since unique PCR fragments were 300-800 bp (see column 50).

Regarding claims 45, 87, 223, and 247, the organism could be human (see column 37, last paragraph).

Regarding claims 225, 249, 265, 268, and 274, a drug exposure to the cell was considered as a perturbation (see columns 27-29 and 49-52).

Therefore, Friend *et al.,* teach all limitations recited in claims 1, 2, 10-12, 22-26, 28-33, 45, 86, 87, 89, 90, 157-159, 169-173, 175-180, 214, 216, 219-221, 223, 225, 238, 240, 243-245, 247, 249, 265, 268, and 274.

10. Claims 13, 160, 218, and 242 are rejected under 35 U.S.C. 102(e) as being anticipated by Friend *et al.,* as applied to claims 1, 2, 10-12, 22-26, 28-33, 45, 86, 87, 89, 90, 157-159, 169-173, 175-180, 214, 216, 219-221, 223, 225, 238, 240, 243-245, 247, 249, 265, 268, and 274 above, in light of Roninson *et al.,* (US Patent No.5,811,234, published on September 22, 1998).

The teachings of Friend *et al.,* have been summarized previously, *supra*. However, Friend *et al.,* did not disclose to a cDNA having at least 1000 different genes as recited in claims 13, 160, 218, and 242. Since Roninson *et al.,* showed that somatic tissues of higher eukaryotes expressed mRNA for about 10,000 genes (see example 9 in columns 15 and 16), a cDNA library made by Friend *et al.,* also considered to have at least 1000 different genes as recited in claims 13, 160, 218, and 242.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 27, 174, 222, and 246 are rejected under 35 U.S.C. 103(a) as being unpatentable over Friend *et al.,* (1998) as applied to claims 1, 2, 10-12, 22-26, 28-33, 45, 86, 87, 89, 90, 157-159, 169-173, 175-180, 214, 216, 219-221, 223, 225, 238, 240, 243-245, 247, 249, 265, 268, and 274 above.

The teachings of Friend *et al.,* have been summarized previously, *supra.*

Friend *et al.,* did not disclose to the limitations recited in claims 27, 174, 222, and 246..

However, in the absence of unexpected results, it would have been obvious to one having ordinary skill in the art at the time the invention was made to have immobilized different length of polynucleotide probes on an array as recited in claims 27, 174, 222, and 246 in view of patents of Friend *et al...* One having ordinary skill in the art has been motivated to modify the method of Friend *et al.,* because optimization of the length of immobilized polynucleotide probes on an

array would have been obvious to one having ordinary skill in the art at the time the invention was made. One having ordinary skill in the art at the time the invention was made would have been a reasonable expectation of success to optimization of the length of immobilized polynucleotide probes on an array. Note that Where the general conditions of a claim are disclosed in the prior art, it is not inventive, in the absence of an unexpected result, to discover the optimum or workable ranges by routine experimentation. *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

13. Claims 14-21 and 161-168 are rejected under 35 U.S.C. 103(a) as being unpatentable over Friend *et al.,* (1998) as applied to claims 1, 2, 10-12, 22-26, 28-33, 45, 86, 87, 89, 90, 157-159, 169-173, 175-180, 214, 216, 219-221, 223, 225, 238, 240, 243-245, 247, 249, 265, 268, and 274 above, further in view of Chee *et al.,* (US Patent No. 6,355,431B1, prior date: May 20, 1999).

The teachings of Friend *et al.,* have been summarized previously, *supra*.

Friend *et al.,* did not disclose to the limitations recited in claims 14-21 and 161-168.

Chee *et al,* teach the limitations recited in claims 14-21 and 161-168 (see columns 39 and 40).

Therefore, in the absence of unexpected results, it would have been obvious to one having ordinary skill in the art at the time the invention was made to have immobilized different amount of polynucleotide probes on an array as recited in claims 14-21 and 161-168 in view of patents of Friend *et al.,* and Chee *et al.*. One having ordinary skill in the art has been motivated to modify the method of Friend *et al.,* and combine above methods together because optimization

of amount of immobilized polynucleotide probes on an array would have been obvious to one having ordinary skill in the art at the time the invention was made. One having ordinary skill in the art at the time the invention was made would have been a reasonable expectation of success to optimization of amount of immobilized polynucleotide probes on an array. Note that Where the general conditions of a claim are disclosed in the prior art, it is not inventive, in the absence of an unexpected result, to discover the optimum or workable ranges by routine experimentation. *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

Conclusion

14. No claim is allowed.

15. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is either (703) 308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (703) 305-1270. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application should be directed to the patent Analyst of the Art Unit, Ms. Chantae Dessau, whose telephone number is (703) 605-1237.

Frank Lu
October 1, 2002

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600